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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/137,059	08/20/1998	BRIAN JOHNSTON	A-65200/WHD/	2454

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MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/137,059	JOHNSTON ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-49* is/are pending in the application.

4a) Of the above claim(s) *29-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-28 and 32-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08-03-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 23-28 and 32-49 are currently under examination, Applicants withdrew claims 29-31 as being drawn to a non-elected invention.

Response to Arguments

Claim Rejections - 35 USC § 102

3. Claims 23-28, 33 and 37 remain rejected under 35 U.S.C. 102(e) as being anticipated by Bekkaoui et al. (U.S. Patent 6,136,533) as evidenced by Shih et al. (US 5,589,332) for the same reasons of record as set forth in the Official Action mailed 02/27/02, 12/11/02, and those reasons set forth below.

Applicant's arguments filed 5-03-2004 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that Bekkaoui et al. does not teach a catalytically inactive RNA molecule as claimed. According to Applicants there is also no teaching of catalytic action of an RNA molecule upon a substrate that is dependent on target binding as claimed. Moreover Applicants argue that Bekkaoui et al. is not enabling for target dependent catalysis as claimed, since there is no disclosure of nucleic acid sequences or reaction conditions which would enable one of skill in the art to make and use an RNA construct for target-dependent catalysis towards a substrate in a method for detection of a target molecule as claimed. Contrary to Applicant's assertions, although Bekkaoui et al. does not recite wherein the ribozyme is a catalytically inactive RNA molecule as recited in the instant claims, it is clear and well known in the art, that in order for a ribozyme to cleave a substrate nucleic acid, it must first

be bound by to the substrate. There is no catalytic action, if there is no substrate for a ribozyme to act upon. Therefore, when the ribozyme is not bound to its substrate it is catalytically inactive. Moreover, contrary to Applicant's assertion that Bekkaoui is not enabled for substrate dependent catalysis, the Bekkaoui et al. disclosure provides more than sufficient guidance that would enable the skilled artisan to practice the full scope of the claimed invention. For example, at col. 11, lines 63-67, Bekkaoui et al. lists multiple US Patents which describe related methods for target dependent catalysis. For example, Bekkaoui et al. mentions US Patent No. 5,589,332, Shih et al., this reference clearly describes the conserved nucleic acid target sequence of ribozymes (see Figure 1a), and further describes a system for the use of a ribozyme as a diagnostic tool for detecting the presence of a nucleic acid, protein, or other molecule, in which the formation of an active ribozyme and cleavage of an assayable marker is dependent on the presence or absence of the specific target molecule. Shih et al. also discloses that the essential component is a ribozyme specifically but reversibly binding a selected target in combination with a labelled co-target, preferably immobilized on a support structure. Bekkaoui et al. is therefore considered fully enabled to practice the instantly claimed invention, since at the time of the instant invention the prior art provided sufficient guidance that would enable the skilled artisan to make and use and RNA construct for target dependent catalysis towards a substrate in a method for detecting a target molecule.

Moreover, Applicants argue that the methods of Bekkaoui et al. comprising providing ribosomal protein and/or spermine, and/or a chelator and a detergent in the reaction mixture, however these components are neither required nor claimed in the present invention. Contrary to Applicant's assertions, the claims of the instant invention recite a method "comprising" certain

steps, therefore although the instant claims do not require ribosomal protein and/or spermine, and/or a chelator and a detergent in the reaction mixture, the methods of Bekkaoui et al. are still considered to anticipate the instant invention to the extent that the method is not limited to the particular steps or reactants recited in the instant claims due to the "comprising" language.

4. Claims 23-27, 32-33, 37-43 stand rejected under 35 U.S.C. 102(b) as being anticipated by Stefano et al. (U.S. Patent 5,472,840) for the same reasons of record as set forth in the Official Action mailed 02/27/02, 12/11/02, and those reasons set forth below.

Applicant's arguments filed 12-13-04 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the Stefano reference does not teach wherein the catalytically inactive RNA molecule comprises all nucleotide sequence of a complete catalytic domain. According to Applicants, the instant invention is distinguished over the Stefano reference since the claimed invention includes the nucleotides sequences of a complete catalytic domain that is separate from and independent of target sequences. However, it is noted that the instant claims recite that the catalytically inactive RNA molecule binds to said target molecule, wherein said RNA molecule comprises all nucleotide sequences of a complete catalytic domain, the instant claims do not require that said catalytically inactive RNA molecule comprises all nucleotide sequences of a complete catalytic domain that is separate from and independent of target sequences. The instant claims do not recite the limitation "target sequences," the claims recite "target molecule," which may encompass compounds other than nucleic acid sequences. For example, Stefano teaches that ribozyme dependent catalytic active dependent upon the presence of divalent cation, such as Mg+2. To this extent, it remains that the Stefano reference is considered to anticipate the instant invention.

As stated in the prior Office Action, the RNA target molecule 11 of Figure 1A of Stefano comprises a region 29 that forms the catalytic region of a ribozyme, once bound to the first nucleic acid 31, however, Stefano further teaches that this structure requires a divalent cation co-factor for its activity. Moreover, Stefano teaches that the first nucleic acid also comprises an autocatalytic replication region, wherein said region does not become activated until the first nucleic acid is bound to the target, wherein a ribozyme is formed, and said ribozyme (once exposed to divalent cation, Mg+2) becomes active, cleaves at position 39, and releases the autocatalytic replication region from said first nucleic acid. The presence of the RNA target molecule in a composition is determined by monitoring for the presence of the autocatalytic replication reaction product, which is indicative of the presence of the target molecule. Applicant's arguments are not persuasive.

It was not previously indicated by the examiner that the capture probe may comprise a terminal biotinylated nucleotides, and wherein the solid support comprises streptavidin-coated particles target molecules complementary to another portion of the target RNA may be conveniently captured upon an immobilized streptavidin support (see col. 8, lines 42-44), the streptavidin, may also include streptavidin-derivatized paramagnetic particles (see page 35, line 10).

5. Claims 23-28, and 32-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Shih et al. (US Patent No. 5,589,332).

Shih et al. describe a ribozyme amplified diagnostic (RAD) methodology that includes three principal components: a ribozyme, with one arm designed to base-pair with labeled RNA molecules bearing an NUX cleavage site and referred to as the "co-target" which are anchored to

a solid support, and the other arm of ribozyme to base-pair with a predetermined sequence on the RNA being detected, the "target" RNA. When the ribozyme cleaves the co-target RNA, a portion of the co-target remains bound to the support and the labeled NUX-bearing portion is released. Release of label from an unknown sample allows the determination of the approximate number of target molecules present; i.e., by constructing a standard curve of the cleavage of the co-target in the presence of varying amounts of target, one can determine the approximate number of target molecules present in the sample (see col. 5, lines 5-24). The ribozymes used in the methods of Shih et al. may also comprise hairpin structures and hammer head ribozymes (see Figures 1a-5b.

Conclusion

6. Claims 44-49 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Janet L. Epps-Ford, Ph.D.
Patent Examiner
Art Unit 1635

JLE